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REMARKS

Status of the Claims

Claims 87-93 and 110-113 are pending in the application.

Claims 87-93 and 110-113 are provisionally rejected under the doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 11, 13, 14, and 16 of co-pending Application No. 09/310,735 (hereinafter, the "735 application"). Claims 87-93 are rejected under 35 U.S.C. § 102(b) as being anticipated by McKnight *et al.*, *Immunogenetics,* **1989**, *30*, 145-47. Claims 87-93 are rejected under 35 U.S.C. § 102(b) as being anticipated by Chen *et al.*, *Proc. Natl. Acad. Sci. USA,* **1985**, *82*, 7284-7288. Claims 87-91 are rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,090,620. Claims 110-113 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility. Claims 110-113 are rejected under 35 U.S.C. § 112, first paragraph.

Applicants use the paragraph numbering in the Office Action (Paper No. 26) in responding to the examiner's remarks.

2.-3. Double Patenting

Claims 87-93 and 110-113 were provisionally rejected under the doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 11, 13, 14, and 16 of co-pending Application No. 09/310,735 (hereinafter, the "735 application"). The Office Action alleges that although the conflicting claims are not identical, they are not patentably distinct. Applicants traverse the rejection of claims 87-93 and 110-113 and request reconsideration thereof.

An obviousness-type double patenting rejection is analogous to a failure to meet the nonobviousness requirement of 35 U.S.C. § 103. *In re Braithwaite*, 154 U.S.P.Q. 29, 34 (C.C.P.A. 1967) and *In re Longi*, 225 U.S.P.Q. 645, 648 n.4 (Fed. Cir. 1985). In making an obviousness-type double patenting analysis, then, the proper inquiry is as taught in *Graham v. John Deere Co.*, 383 U.S. 1 (1966). See, M.P.E.P. §804.

Claims 11, 13, 14, and 16 of the '735 application are drawn to compounds identified by particular methods for identifying compounds that modulate activity of target RNAs or target biomolecules. The claims of the '735 application do not recite any of the secondary

structures, joined sequence length, or nucleotide sequences that are recited in the claims of the present application. Thus, the RNA molecules of the present invention, which recite secondary structures, joined sequence lengths, or nucleotide sequences are not obvious variants of the compounds claimed in the co-pending application, which fail to recite any of these elements.

That an RNA molecule of the present invention may fall within the claim scope of the co-pending application is irrelevant. Indeed, a determination whether one patent application is generic to another patent application is not the appropriate inquiry. *In re Kaplan*, 229 U.S.P.Q. 678 (Fed. Cir. 1986).

Thus, that some of Applicants' compounds claimed in the present patent application may also meet limitations of claims in co-pending patent applications (of which Applicants do not concede) is not grounds for an obviousness-type double patenting rejection. It is simply a case of one patent application dominating another patent application. Domination by itself cannot support a double patenting rejection. Thus, the obviousness-type double patenting rejection is misplaced.

In view of the foregoing, Applicants respectfully request that the rejection of claims 87-93 and 110-113 under the doctrine of obviousness-type double patenting be withdrawn.

35 U.S.C. § 102(b)

4. The McKnight Reference

Claims 87-93 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by McKnight *et al.*, *Immunogenetics,* **1989**, *30*, 145-47 (hereinafter, the "McKnight reference"). Applicants traverse the rejection and respectfully request reconsideration thereof because the McKnight reference fails to teach every element recited in the claims.

The McKnight reference reports a cDNA sequence of a rat IL-2 clone that contains a 5' untranslated region, coding region, and 3' untranslated region in Figure 1. In total, the reported cDNA sequence contains 740 nucleotides. The McKnight reference fails to teach any secondary structure associated with the 740 nucleotide cDNA sequence.

The Office Action incorrectly asserts that the McKnight reference teaches an RNA comprising SEQ ID NO:23 and SEQ ID NO:25 and having at least twenty-nine but no more than seventy nucleotides, which contains the secondary structure recited in claim 87. As stated previously, it is undisputed that the McKnight reference fails to disclose any secondary

structure of the 740 nucleotide cDNA sequence reported therein. Nonetheless, the Office Action assumes that the McKnight cDNA comprises the secondary structure recited in claims 87-93. Thus, it appears that the Office Action asserts that the secondary structure recited in Applicants' claims is inherent in the McKnight cDNA sequence. To anticipate a claim, however, a prior art reference must disclose every feature of the claimed invention, either explicitly or inherently. *Glaxo v. Novopharm, Ltd.*, 334 U.S.P.Q.2d 1565 (Fed. Cir. 1995). Further, to serve as an anticipation when a reference is silent about the alleged inherent characteristic, such gap in the reference may be filled by extrinsic evidence. Such evidence, however, must make clear that the missing descriptive matter is necessarily (*i.e.*, always) present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill in the art. *In re Oelrich*, 40 U.S.P.Q. 323 (C.C.P.A. 1981); *Continental Can Co. USA Inc. v. Monsanto Co.*, 20 U.S.P.Q.2d 1746 (Fed. Cir. 1991). Inherency may not be established by probabilities or possibilities. *Id.* Further, the mere fact that a certain thing may result from a given set of circumstances is not sufficient. *Id.* Significantly, the Office Action has not established that the critical inherent characteristics are necessarily present in the McKnight reference. Indeed, the Office Action fails to provide any extrinsic evidence that makes clear that the missing descriptive matter is always present in the thing described in the McKnight reference, and that it would be so recognized by persons of ordinary skill in the art.

Regardless of whether the cDNA sequence reported in the McKnight reference comprises the secondary structure recited in claim 87 (and Applicants submit that the Office Action utterly fails to establish that such secondary structure is inherent in the reported cDNA sequence), the McKnight reference fails to teach an RNA comprising "not more than seventy nucleotides." A prior art reference anticipates a claim if every element of the claim appears in the prior art reference. *Glaxo Inc. v. Novopharm, Ltd.*, 52 F.3d 1043, 1047, 34 U.S.P.Q.2d 1565, 1567 (Fed. Cir. 1995). Because the cDNA sequence reported in the McKnight reference is 740 nucleotides in length, it does not anticipate claim 87 (nor dependent claims 88-93), which recites an RNA "not more than seventy nucleotides."

The Office Action takes the view that due to the use of the word "comprising," the claims read on sequences that are longer than 70 nucleotides. Applicants respectfully disagree and submit that the Examiner cannot consider individual terms recited in a claim and interpret them in a vacuum. Claim 87 states, in part, "An RNA comprising a joined sequence of at least twenty-nine ***but not more than seventy nucleotides*** ..." (emphasis added). Claim 87,

therefore, recites that the joined sequence ranges from twenty-nine to seventy nucleotides. The position taken by the Examiner completely vitiates the explicit language recited in the claim. The term "comprising" relates to other components of the RNA that do not involve the overall number of nucleotides in the sequence. Indeed, an RNA that has forty nucleotides and the secondary structure recited in claim 87 in addition to, for example, a radiolabel would infringe claim 87. Thus, the McKnight reference does not disclose an RNA that comprises a joined sequence of "at least twenty-nine but not more than seventy nucleotides" and, therefore, does not anticipate the claimed inventions.

In view of the foregoing, the McKnight reference fails to anticipate claims 87-93. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

5. The Chen Reference

Claims 87-93 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Chen *et al.*, *Proc. Natl. Acad. Sci. USA,* **1985**, *82*, 7284-7288 (hereinafter, the "Chen reference"). Applicants traverse the rejection and respectfully request reconsideration thereof because the Chen reference fails to teach every element recited in the rejected claims.

The Chen reference reports a cDNA sequence of a human IL-2 clone and two gibbon IL-2 clones that contains a 5' untranslated region, coding region, and 3' untranslated region in Figure 3. In total, the reported cDNA sequences each contain from about 800 to 1000 nucleotides. The Chen reference fails to teach any secondary structure associated with the cDNA sequences reported therein.

In similar fashion to the rejection over the McKnight reference, the Office Action incorrectly asserts that the Chen reference teaches an RNA comprising SEQ ID NO:24 and having at least twenty-nine but no more than seventy nucleotides, which contains the secondary structure recited in claim 87. Regardless of whether the cDNA sequences reported in the Chen reference comprise the secondary structure recited in claim 87 (and Applicants submit that the Office Action utterly fails to establish that such secondary structure is inherent in the reported cDNA sequences), the Chen reference fails to teach an RNA comprising "not more than seventy nucleotides." As stated above, a prior art reference anticipates a claim if every element of the claim appears in the prior art reference. Because the cDNA sequences reported in the Chen reference are at least 800 to 1000 nucleotides in length, it does not anticipate claim 87 (nor dependent claims 88-93), which recites an RNA

"not more than seventy nucleotides." Further, as discussed above, use of the term "comprising" in the claims does not vitiate the phrase "at least twenty-nine but not more than seventy nucleotides."

Claims 87-93 recite an RNA having a particular secondary structure. It is undisputed that the Chen reference fails to disclose any secondary structure of the at least 800 nucleotide cDNA sequences reported therein. Nonetheless, the Office Action assumes that the Chen cDNA comprises the secondary structure recited in claims 87-93. Thus, it appears that the Office Action asserts that the secondary structure recited in Applicants' claims is inherent in the Chen cDNA sequence. As stated above, to anticipate a claim, a prior art reference must disclose every feature of the claimed invention, either explicitly or inherently, and any gaps may be filled by extrinsic evidence. Significantly, the Office Action has not established that the secondary structure recited in the claims is necessarily present in the Chen reference. Indeed, the Office Action fails to provide any extrinsic evidence that makes clear that the missing descriptive matter is always present in the thing described in the Chen reference, and that it would be so recognized by persons of ordinary skill in the art. Thus, Office Action has failed to establish that the Chen reference anticipates claims 87-93.

In view of the foregoing, the Chen reference fails to anticipate claims 87-93. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

6. The Fu Reference

Claims 87-91 were rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 6,090,620 (hereinafter, the "Fu reference"). Applicants traverse the rejection and respectfully request reconsideration thereof because the Fu reference fails to teach every element recited in the rejected claims.

The Examiner continues to assert that the Fu reference teaches genomic DNA encoding the WRN gene, which encodes RNA comprising SEQ ID NOs:23 and 25, having at least twenty-nine but not more than seventy nucleotides. The only sequence within the Fu reference that the Examiner specifically identifies is nucleotides 26015 to 26041 within SEQ ID NO:209, which is AGTTTCTTTTTGGAAGCACTTAGAGCT and which is only twenty-seven nucleotides in length. SEQ ID NO:209 reported in the Fu reference is 51,259 nucleotides long.

In regard to claims 87-91, in similar fashion to the rejections over the McKnight and Chen references, the Office Action incorrectly asserts that the Fu reference teaches an RNA comprising SEQ ID NOs:23 and 24, and having at least twenty-nine but no more than seventy nucleotides, which contains the secondary structure recited in claim 87. Regardless of whether the DNA sequence reported in SEQ ID NO:209 of the Fu reference comprises the secondary structure recited in claim 87 (and Applicants submit that the Office Action utterly fails to establish that such secondary structure is inherent in the reported DNA sequence), the Fu reference fails to teach an RNA comprising "not more than seventy nucleotides." As stated above, a prior art reference anticipates a claim if every element of the claim appears in the prior art reference. Because the DNA sequences reported in the Fu reference contains more than 50,000 nucleotides, it does not anticipate claim 87 (nor dependent claims 88-91), which recites an RNA "not more than seventy nucleotides." Further, it is not even clear how the cited portion of the genomic DNA sequence reported in SEQ ID NO:209 of the Fu reference encodes RNA comprising SEQ ID NOs:23 and 25. Further, as discussed above, use of the term "comprising" in the claims does not vitiate the phrase "at least twenty-nine but not more than seventy nucleotides."

Claims 87-91 recite an RNA having a particular secondary structure. It is undisputed that the Fu reference fails to disclose any secondary structure for the 50,000+ nucleotide sequence of SEQ ID NO:209 or the cited portion thereof. Nonetheless, the Office Action assumes that the Fu DNA comprises the secondary structure recited in claims 87-91. Thus, it appears that the Office Action asserts that the secondary structure recited in Applicants' claims is inherent in the Fu DNA sequence. As stated above, to anticipate a claim, a prior art reference must disclose every feature of the claimed invention, either explicitly or inherently, and any gaps may be filled by extrinsic evidence. Significantly, the Office Action has not established that the secondary structure recited in the claims is necessarily present in the Fu reference. Indeed, the Office Action fails to provide any extrinsic evidence that makes clear that the missing descriptive matter is always present in the thing described in the Fu reference, and that it would be so recognized by persons of ordinary skill in the art. Thus, Office Action has failed to establish that the Fu reference anticipates claims 87-91.

In view of the foregoing, the Fu reference fails to anticipate claims 87-91. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 102(e) be withdrawn.

7.-8. 35 U.S.C. § 101

Claims 110-113 were rejected under 35 U.S.C. § 101 because the claimed invention is allegedly not supported by either a specific or substantial asserted utility or a well established utility. Applicants traverse the rejection.

Claims 110-113 have a specific utility for the subject matter claimed and a substantial utility that defines a "real world" use. The specific and substantial utility as defined in the specification is to identify "particular structural elements in eukaryotic and prokaryotic nucleic acid that are molecular interaction sites. ... and methods of identifying particular structural elements in eukaryotic and prokaryotic nucleic acid, especially RNA molecules, which can interact with other molecules *to effect modulation* of the RNA. *'Modulation' refers to augmenting or diminishing RNA activity or expression.*" Emphasis added. See specification, for example, page 32, l. 29 to page 33, l. 1. A specific utility is to modulate an "exemplary RNA target," for example, IL-2 mRNA for therapeutic treatment of inflammation. See specification, e.g., Table 1, page 38, l. 9.

The specific and substantial utility applies to claims 110-113 which include SEQ ID NO: 23, 24, and 25. These sequences comprise a portion of the 3' UTR of interleukin-2 mRNA. These sequences are useful for modulating levels of IL-2 mRNA, for example, by decreasing expression of IL-2 protein and reducing inflammation in a patient treated with purified and isolated RNA fragments of claims 110-113.

In view of the foregoing, the claimed invention is well supported by a specific and substantial asserted utility. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 101 be withdrawn.

9. 35 U.S.C. § 112, first paragraph

Claims 110-113 were rejected under 35 U.S.C. § 112, first paragraph. The Office Action alleges that since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would allegedly not know how to use the claimed invention. Applicants traverse the rejection.

Applicants have provided a specific, substantial and credible utility as stated above. Applicants have also provided sufficient disclosure that one skilled in the art can make and use Applicants' claimed invention. Claims 110-113 provide specific RNA sequences useful for augmenting or diminishing IL-2 mRNA expression. Claim 110 encompasses a purified

and isolated RNA fragment, a consensus sequence, conserved across two species (SEQ ID NO: 23). Claim 111 encompasses a purified and isolated RNA fragment comprising a specific human sequence (SEQ ID NO: 24). Claim 112 encompasses a purified and isolated RNA fragment comprising a specific mouse sequence (SEQ ID NO: 25). Claim 113 encompasses a purified and isolated RNA fragment comprising a specific rat sequence (SEQ ID NO: 25). See specification, for example, page 152, lines 21-29. The specification teaches that one may use these isolated and purified RNA fragments to modulate expression of IL-2 and control inflammation in a mammalian subject.

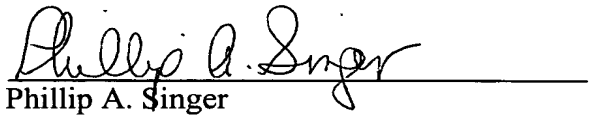
In view of the foregoing, one skilled in the art would clearly know how to use the claimed invention. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 112, paragraph 1, be withdrawn.

Conclusion

In view of the foregoing, Applicants respectfully submit that the finality of the Office Action should be withdrawn, and that the claims are in condition for allowance. An early notice of all chance is solicited. The Examiner is invited to contact Applicants' undersigned representative at (206) 332-1380 if there are any questions regarding Applicants' claimed invention.

Respectfully submitted,

Date: December 20, 2002



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